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10/526,120	07/14/2005	**Kaw Yan Chua**	11747.105002 NUS002	2575

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	
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09/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,120	CHUA ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed on 05/28/209 is acknowledged.

2. Claims 16-20 and 23-27 are currently under examination as they read on a method for immunization against an allergen comprising administering to a subject the recombinant nucleic acid of SEQ ID NO:5 and Der p I to the subject by intramuscular administration.

3. In view of the amendments filed on 05/28/209, only the following rejections are maintained.

Claim Objections

4. Claims 25 stands objected to because of the following informalities: Claim 25 is dependent upon cancelled base claims 1-13. Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 16-20 and 23-27 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and

wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year; does not reasonably provide enablement for: a method for immunization against an allergen comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding the allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum and in a second phase administering the allergen to the subject of claims 16-20 and 23; A method for immunization against **an allergen** comprising administering to a subject a nucleic acid comprising **an expressible allergen gene** in a first phase over a period of about a year so as to induce long term immune *memory* in the subject; and administering **the allergen** to the subject in a second phase of claim 24 or a method for treating or **preventing** an allergic reaction in a subject comprising administering to a subject in a first phase a recombinant nucleic acid to a subject wherein the recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum of claims 25-27. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons as set forth in the Office Action mailed on 11/28/2008.

Applicant's arguments filed on 05/28/209 have been fully considered, but are not found persuasive.

Applicant argues:

"....the Examiner asserts that allergens other than the Der p 1 sequence of SEQ ID NO: 5 and the native Der p 1 protein are not enabled because the specification fails to provide guidance regarding which allergen sequences other than the Der p 1 sequence of SEQ ID NO: 5 and the native Der p 1 protein would work in the claimed invention. Applicants must disagree with the Examiner's assertion because paragraph [0041] of the specification provides a list of all the allergens that would work in the claimed invention; these include Blo t 1, BIot 5, Der p 1, Der p 2, Der p 3, Der f 1, Der f2 and Der f 3. Furthermore, Examples 3 and 4 as well as Figs. 1 to 8 are all directed to the allergen Blot 5. The Blo t 5 gene is comprised within the recombinant nucleic acids SEQ ID NOs: 2, 3 and 4 (see also paragraphs [0096], [0097] and [0098]). Hence, contrary to the Examiner's assertion, Applicants submit that the specification clearly provides sufficient guidance and working examples on allergen sequences other than the Der p 1 sequence of SEQ ID NO: 5 and the native Der p I protein that would work m the claimed invention. Accordingly, Applicants submit that the specification is enabling for whole allergens other than the Der p 1 sequence of SEQ ID NO: 5 and the native Der p I protein, and that the scope of the claims should not be limited only to the Der p 1 sequence of SEQ ID NO: 5 and the native Der p 1 protein.

The Examiner also asserts that the structures of all the allergens are not known, and hence the present claims would encompass presently as yet unidentified allergens. Applicants submit that the cloning and sequencing of genes in general are routine and known to those skilled in the art. Furthermore, paragraph [0041] of the specification lists several exemplary publications that would provide sufficient guidance to those skilled in the art to clone and sequence allergen genes for use in the recombinant nucleic acids of the claimed invention."

".....the Examiner asserts that the specification is not enabled for all recombinant nucleic acids encoding the genus of all the aforementioned allergens. Applicants submit that paragraph [0041] teaches house dust mite species, the genes of which would work in the present invention. These are *Blomia tropicalis, Dermatophagoides pteronyssinus, and Dermatophagoides farinae.* Furthermore, as noted above, paragraph [0041] of the specification lists several exemplary publications that would provide sufficient guidance to those smiled in the art to clone and sequence allergen genes, regardless of genus/species, for use in the recombinant nucleic acids of the claimed invention.

."......the specification does provide exemplary "signal" and "target" peptides *from Rattus norveg~cus* (see for example SEQ ID NOs: 7, 8, 23, 24, 27, 28, 43, 44), *Mus musculus* (see for example SEQ 133 NOs: 2-5, 11-12, 15, 16, 25, 26, 31, 32, 35, 36, 45, 46), and *Homo sapiens(see* for example SEQ ID NOs: 6, 9, 10, 13, 14, 17-22, 29, 30, 33, 34, 37-42, 47, 48). Figs. 3-10 and Examples 3 to 5 teach the use of the LAMP-I signal peptide from *Mus musculus,* while Figs. 11-12 and Example 6 teach use of the *Homo sapiens* tissue plasminogen activator signal peptide from *Homo sapiens* (SEQ ID NO: 6).

"..... Claim 25 is amended to read as "In] method for treating or prophylaxis of an allergic reaction .... " A prophylactic result can be the inhibition of the rate of a reaction or allergic disease onset or progression (see paragraph [0072]) and not necessarily a 100% prevention is required. Furthermore, prophylactically effective amounts are taught in for example paragraph [0073]; these are from about 100 μg to 5000 μg, preferably 200 μg to 2000 μg."

"In view of the above, Applicants submit that the Examiner is incorrect to assert that the specification is only enabling for a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO: 5 by intramuscular administration and the native Der p 1 allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant, wherein the nucleic acid is administered m the first phase over a period of time sufficient to induce long terra immune memory in the subject, and wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year. Recombinant nucleic acids other than SEQ ID NO: 5 (such "as SEQ ID NOs: 2, 3, 4 and 6, comprising various combinations of exemplary signal peptides, allergens, and target peptides as discussed above) are clearly taught in the present specification. Administration of these recombinant nucleic acids via other routes (i.e. other than the intramuscular route) such as the intradermal route (see paragraphs [00901, [01151) and oral route (see paragraphs [0092], [0127]) are also clearly taught

in Examples 3 and 6. Allergens other than Der p 1, such as Blot 1, Blot 5, Der p 2, Der p 3, Der f 1, Der f 2 and Der f 3 axe also taught as set out above - see m particular Figs. 3 to 8 and Example 3 where the Blot 5 protein is used.

It remains the Examiner's position that the specification discloses only a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year. Applicant's assertion that paragraphs 96-98 teach the method with Blo t 5 gene within the recombinant nucleic acids SEQ ID NOs: 2, 3 and 4 is unfounded because the nucleic acids were never administered. There is no evidence whatsoever that the nucleic acids of SEQ ID NOs 2-4 would immunize against an allergen, and/or treat or prevent an allergic reaction.

It also remains the Examiner's position that the instant claimed reads on the administration all whole allergens and all recombinant nucleic acids encoding the genus of all allergens. The structures of all allergens are not known therefore the instant claim recitations encompass allergens presently unidentified by scientists. Contrary to Applicant's assertion, it is undue experimentation to discover, clone and sequence all undiscovered allergens and to determine the genus of all possible nucleic acids encoding them. The specification fails to provide guidance regarding which allergen sequences other than the Der p I sequence of instant SEQ ID NO:5 and the native Der p I protein can work in the claimed invention. Therefore,

claims encompassing the genus of all discovered and undiscovered allergens are not enabled.

It also remains the Examiner's position that the specification has not adequately disclosed the genus of all "signal peptides" for use in the claimed invention. Without a specific, limiting definition in the specification, these terms encompass the genus of all peptides. The specification has not adequately disclosed the genus of all signal peptides for use in the claimed invention. The specification only discloses immunization with the *Mus musculus* N-terminal signal peptide of LAMP-1, the entire Der p I gene product and the *Mus musculus* transmembrane and cytoplasmic domain of SEQ ID NO:5. The specification does not adequately support the genus of methods of administering any allergen encoding nucleic acid with any signal peptide that mediates translocation of the allergen into the endoplasmic reticulum to immunize, treat or prevent allergy. One of ordinary skill in the art would be required to perform undue experimentation to determine which amino acid sequences are meant to be encompassed by the instant signal peptides and what nucleic acids encode them.

It also remains at issue whether or not the claimed method would function to "prevent" allergy. Applicant is arguing limitations that are not present in the claims because the claims are not directed to "a method for treating or prophylaxis of an allergic reaction" as asserted by Applicant. The claims as submitted on 05/28/2009 are still directed to treating or preventing allergic reactions and the specification provides no in vivo data to support the claimed subject matter. Therefore, the specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of allergy by administering the claimed compositions.

Therefore, the rejection is maintained.

7. Claims 16-20 and 23-27 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant; wherein the nucleic acid is administered in the first phase over a period of time sufficient to induce long term immune memory in the subject; and wherein multiple doses of the nucleic acid is administered in the first phase over a period of about a year.

Applicant is not in possession of**:** a method for immunization against an allergen comprising administering to a subject in a first phase a recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding the allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum and in a second phase administering the allergen to the subject of claims 16-20 and 23; A method for immunization against **an allergen** comprising administering to a subject a nucleic acid comprising **an expressible allergen gene** in a first phase over a period of about a

year so as to induce long term immune *memory* in the subject; and administering **the allergen** to the subject in a second phase of claim 24 or a method for treating or **preventing** an allergic reaction in a subject comprising administering to a subject in a first phase a recombinant nucleic acid to a subject wherein the recombinant nucleic acid comprising a gene encoding **a first signal peptide** operably linked to **a gene encoding an allergen** wherein the **first signal peptide** mediates the translocation of **the allergen** into the endoplasmic reticulum of claims 25-27 for the same reasons as set forth in the Office Action mailed on 11/28/2008.

Applicant's arguments filed on 05/28/2009 have been fully considered, but are not found persuasive.

Applicant argues:

"Applicants must again respectfully disagree with the Examiner for the reasons already set out above in Section (B) above regarding the enablement rejection. Applicants respectfully assert that the Examiner is construing the written description requirement too stringently.

Applicants re-iterate that other recombinant nucleic acids (SEQ ID NOs: 2-4, 6) are clearly taught and described in the present specification. SEQ ID NO: 2 is directed to a recombinant nucleic acid that comprises the *Mus musculus* LAMP-I leader sequence, the Blot 5 gene fragment for the H-2J-restricted Th epitope and the *Mus musculus* LAMP-1 transmembrane and cytoplasmic domain. SEQ ID NO: 3 is directed to recombinant nucleic acid that comprises the *Mus musculus* LAMP-I leader sequence, the entire Blot 5 gene *and the Mus musculus* LAMP-1 transmembrane and cytoplasmic domain. SEQ ID NO: 4 is directed to a recombinant nucleic acid that comprises *the Mus musculus* LAMP-I leader sequence and the entire Blot 5 gene. SEQ ID NO: 6 is directed to a recombinant nucleic acid that comprises the *Homo sapiens* tissue plasminogen activator leader sequence, the entire Der p 1 gene and the *Mus musculus* LAMP-1 transrnembrane and cytoplasmic domain. See also paragraphs [0044] and paragraphs [0045] - [0046] describing promoters that could be used in these recombinant nucleic acids and methods of construction of these recombinant nucleic acids, as well as paragraphs [0096] - [0098] and [0100] that describe the structural make-up of these recombinant nucleic acids. The functions and activity of these recombinant sequences are demonstrated in Figs. 3-8 and 11-12 and Examples 3~ 4 and 6.

Applicants also re-iterates the above submission that other allergens (i.e. other than Der p 1) such as Blo t 1, Blot 5, Der p 2, Der p 3, Der f 1, Der f2 and Der f3 are dearly taught and described in the present specification. In particular, the Blot 5 allergen (SEQ ID NO: 50) has

been used in the various recombinant nucleic acid constructs as set out above, in Examples 3 and 4 and in Figs. 1-8. "

It remains the Examiner's position that the specification discloses a method for immunization against an allergen comprising administering the recombinant nucleic acid of SEQ ID NO:5 by intramuscular administration and the native Der p I allergen to the subject intraperitoneally and subsequently by aerosol in combination with an adjuvant. Other than the specific recombinant nucleic acid of SEQ ID NO:5 and Der p I allergen, there is inadequate written description of the structure and functions for any other recombinant nucleic acids and allergens as set forth in the claims.

It is the Examiner's position that the specification does not disclose a correlation between the structure of nucleic acids encoding an allergen and a signal peptide and the functions (immunization against an allergen; treatment and prevention of an allergic reaction; and mediates the translocation of the allergen into the endoplasmic reticulum) such that a skilled artisan would have known what nucleic acids possess the claimed functions. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" Ex parte *Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)), at page 16. In this instant case Applicants have not provided any guidance as to what nucleic acids encoding any allergen and any signal peptide will result in the claimed functions. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17. In the instant case, definition by function does not suffice to define the genus because it is only an indication of what the nuclei acids do rather than

what they are.

Therefore, the rejection is maintained.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 28, 2009

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Maher M. Haddad/

Primary Examiner, Art Unit 1644